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Receptor Specific Peptide Imaging

Cancer remains a major health problem of mankind. Although extensive new knowledge has led health care professionals to a changing philosophy in its management, one factor remains of undisputed importance is early diagnosis. CT and MRI have improved diagnostic abilities for anatomic localization of tumors. However, metabolic or receptor specific tumor imaging is more advanced with nuclear medicine than with CT or MRI.

Vasoactive Intenstinal Peptide (VIP) is a naturally occurring 28 amino acid peptide with a wide range of biological activities. VIP receptors are expressed on a variety of malignant tumor cells, and VIP receptor density is higher than that for somatostatin. Our aims were to label VIP with Tc-99m -generator-produced, radionuclide that possesses ideal characteristics for scintigraphic imaging and to evaluate Tc-99m-VIP for its bioactivity and ability to detect tumors. VIP_{28} was modified at the carboxy terminus by the addition of four amino acids which provided a N_4 configuration for a strong chelation of Tc-99m. To eliminate steric hindrance, 4-aminobutyric acid (Aba) was used as a spacer. Biological activity of the modified VIP_{28} agonist (TP 3654) was examined *in vitro* by using a cell-binding assay, and opossum internal anal sphincter (IAS) smooth muscle relaxivity assay.

Eight patients (M/F, 18-59 yrs) with known or suspected tumors received, i.v. ~ 10 mCi Tc-99m-VIP analog (5 ug TP 3654, specific activity $11x10^3$ Ci/m mol) prepared using an instant kit. Vital signs were recorded and serial spot views or whole body images were obtained for up to 24 hours. Tumor diagnosis was determined with CT, MRI, Tc-99m-SestaMIBI and or histopathology.

Biological activity of TP 3654 was equivalent to that of native VIP. Kits were stable for several months. Free Tc-99m or colloid were <3%. There were neither adverse reactions seen, nor changes in blood pressure or heart rate. Early renal clearance and hepatobiliary excretion at 2-3 hrs were evident. Tc-99m-TP 3654 images were maximally positive 10-30 min. post-administration with high contrast in 2/2 pts with breast cancer, 1/1humeral metastasis of adenocarcinoma, 1/1 with osteosarcoma of the femur, 1/1 with high grade spindle cell sarcoma, and 1/1 with hemangiopericytoma. A clear cell carcinoma of the uterus metastatic to lung was not seen on Tc-99m-TP3654 scan, possibly due to small size. A true negative image was seen in a patient with colorectal cancer which had been surgically removed. All images corroborated with CT, MRI, MIBI, and/or histopathology, except for the high grade spindle cell sarcoma, which was negative on MIBI. VIP analog Tc-99m-TP3654 shows promise as an agent for imaging tumors in humans.